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By: Debra A DeBello
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

James C. Paulson *et al.*

Serial No.: Divisional of 09/007,741

Filed: HEREWITH

For: PRACTICAL *IN VITRO* SIALYLATION OF RECOMBINANT GLYCOPROTEINS

Examiner of Parent Application: Manjunath Rao

Art Unit: 1652

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, please amend the application as follows.

In the Specification:

Page 1, line 8, after the word "application," please add --is a divisional of U.S. Patent Application No. 09/007,741, filed January 15, 1998, pending, which --.

Page 1, line 9, delete "is" and add – both are--, and delete "its" and add --their--.

At page 2, line 9, insert --the-- between "Although" and "impact".

At page 3, line 12, change "nomemclature" to --nomenclature--.

At page 4, line 5, change "N-acetylgalacto" to --N-acetylgalactosaminyl--.

At page 4, line 7, change "N-acetylgluco" to --N-acetylglucosaminyl--.

In the Claims:

Please cancel claims 1-11, 21, 22, 32-43, and 54 without prejudice or disclaimer.

Please add the following new claims 59-97:

59. (New) A method for *in vitro* sialylation of terminal galactose residues present on a glycoprotein, said method comprising contacting said glycoprotein with a reaction mixture that comprises a sialyltransferase, wherein the sialyltransferase is a bacterial sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity, for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said terminal galactose residues, wherein a greater percentage of terminal galactose residues are sialylated compared to an unaltered glycoprotein.

60. (New) The method of claim 59, wherein at least 80% of the terminal galactose residues present on the glycoprotein are sialylated.

61. (New) The method of claim 60, wherein at least 90% of the terminal galactose residues present on the glycoprotein are sialylated.

62. (New) The method of claim 59, wherein the terminal galactose residues comprise one or more saccharides selected from the group consisting of Galβ1,4GlcNAc, Galβ1,4GalNAc, Galβ1,3GalNAc, Galβ1,3GlcNAc, Galβ1,3Ara, Galβ1,6GlcNAc, and Galβ1,4Glc.

63. (New) The method of claim 62, wherein the terminal galactose residues comprise Galβ1,4GlcNAc or Galβ1,3GlcNAc.

64. (New) The method of claim 63, wherein at least 80% of the terminal Galβ1,4GlcNAc residues present on the glycoprotein are sialylated.

65. (New) The method of claim 63, wherein at least 80% of the terminal Galβ1,3GlcNAc residues present on the glycoprotein are sialylated.

66. (New) The method of claim 59, wherein the terminal galactose residues are present on an O-linked oligosaccharide.

67. (New) The method of claim 59, wherein the terminal galactose residues are present on an N-linked oligosaccharide.

68. (New) The method of claim 59, wherein the sialyltransferase includes a sialyl motif which has an amino acid sequence that is at least about 40% identical to a sialyl motif from a sialyltransferase selected from the group consisting of ST3Gal I, ST6Gal I, and ST3Gal III.

69. (New) The method of claim 68, wherein the sialyltransferase is an ST3Gal III.

70. (New) The method of claim 69, wherein the sialyltransferase is a rat ST3Gal III.

71. (New) The method of claim 68, wherein the sialyltransferase is an ST3Gal IV.

72. (New) The method of claim 68, wherein the sialyltransferase is an ST6Gal I.

73. (New) The method of claim 68, wherein the sialyltransferase is an ST3Gal I.

74. (New) The method of claim 59, wherein the bacterial sialyltransferase has an amino acid sequence which is at least 50% identical to an amino acid sequence of a *Neisseria meningitidis* 2,3-sialyltransferase.

75. (New) The method of claim 74, wherein the bacterial sialyltransferase is a *Neisseria meningitidis* 2,3-sialyltransferase.

76. (New) The method of claim 73, wherein the bacterial sialyltransferase has an amino acid sequence which is at least 50% identical to an amino acid sequence of a *Photobacterium damsela* 2,6-sialyltransferase.

77. (New) The method of claim 76, wherein the bacterial sialyltransferase is a *Photobacterium damsela* 2,6-sialyltransferase.

78. (New) The method of claim 59, wherein the bacterial sialyltransferase has an amino acid sequence which is at least 50% identical to an amino acid sequence of a *Haemophilus* 2,3-sialyltransferase.

79. (New) The method of claim 78, wherein the sialyltransferase is a *Haemophilus* 2,3-sialyltransferase.

80. (New) The method of claim 59, wherein the bacterial sialyltransferase has an amino acid sequence which is at least 50% identical to an amino acid sequence of a *Campylobacter jejuni* 2,3-sialyltransferase.

81. (New) The method of claim 80, wherein the sialyltransferase is a *Campylobacter jejuni* 2,3-sialyltransferase.

82. (New) A method for altering the glycosylation pattern of a glycoprotein *in vitro*, the method comprising contacting a glycoprotein-linked saccharide with a galactosyltransferase in the presence of UDP-galactose under suitable conditions for the galactosyltransferase to transfer a galactose residue from the UDP-galactose to the saccharide to form a galactosylated saccharide.

83. (New) The method of claim 82, wherein the galactosylated saccharide comprises one or more saccharides selected from the group consisting of Galβ1,4GlcNAc, Galβ1,4GalNAc, Galβ1,3GalNAc, Galβ1,3GlcNAc, Galβ1,3Ara, Galβ1,6GlcNAc, and Galβ1,4Glc.

84. (New) The method of claim 82, wherein the glycoprotein-linked saccharide comprises a compound of the formula GlcNR'β(1→3)Galβ-OR, wherein:

R is selected from the group consisting of an amino acid, a saccharide, an oligosaccharide or an aglycon group having at least one carbon atom; and

R' is acetyl.

85. (New) The method of claim 82, wherein the glycoprotein comprises a moiety derived from an immunoglobulin.

86. (New) The method of claim 85, wherein the immunoglobulin is an IgG.

87. (New) The composition of claim 82, wherein the glycoprotein is a chimeric protein.

88. (New) The composition of claim 87, wherein the chimeric protein comprises a moiety derived from an immunoglobulin.

89. (New) The method of claim 82, wherein the method further comprises contacting the galactosylated saccharide with a sialyltransferase in the presence of CMP-sialic acid under conditions in which the sialyltransferase catalyzes the transfer of a sialic acid residue from the CMP-sialic acid to the galactosylated saccharide.

90. (New) The method of claim 89, wherein the galactosylating and the sialylating steps are carried out in a single reaction vessel.

91. (New) The method of claim 90, wherein the galactosylating and the sialylating steps are carried out simultaneously.

92. (New) The method of claim 90, wherein the sialyltransferase is added after the galactosyltransferase reaction has neared completion.

93. (New) A composition comprising a glycoprotein which comprises an N-linked or O-linked oligosaccharide, wherein at least about 80% of the terminal oligosaccharides comprise NeuAcα2,3Galβ1,4GlcNAc, NeuAcα2,3Galβ1,3GlcNAc, NeuAcα2,6Galβ1,4GlcNAc, or NeuAcα2,6Galβ1,3GlcNAc.

94. (New) The composition of claim 93, wherein the glycoprotein comprises a moiety derived from an immunoglobulin.

95. (New) The composition of claim 94, wherein the immunoglobulin is an IgG.

96. (New) The composition of claim 93, wherein the glycoprotein is a chimeric protein.

97. (New) The composition of claim 96, wherein the chimeric protein comprises a moiety derived from an immunoglobulin.

REMARKS

Status of the Application

Claims 12-20, 23-31, 44-53, 55-97 are pending with entry of this amendment. Claims 1-11, 21, 22, 32-43, and 54 have been canceled without prejudice. No new matter has been introduced with the newly added claims. Early action on the merits is respectfully requested.

The Amendments

The requested amendments to the specification and claims do not add new matter to the application as originally filed. The amendment at page 2 corrects the inadvertent omission of a word to make the sentence grammatically correct. The amendment at page 3 corrects a typographical error. The amendments at page 4 of the specification provide the correct terminology that corresponds to the "GalNAc" and "GlcNAc" abbreviations. In the originally provided terminology, the "aminyl" suffix was inadvertently omitted. This omission would have been readily apparent to those of skill in the art, as the "N" in "GalNAc" and "GlcNAc" is well known as the symbol for "aminyl."

New claims 59-97 find support in the application as originally filed and therefore do not add new matter to the application.

New claims 59-61 and 64-65 find support in the specification at, for example, page 10 lines 3-11 and claim 12.

New claims 62-63 and 83 find support at, for example, page 12, lines 10-15.

New claims 66 find support at, for example, page 12, lines 15-16.

New claim 67 find support at, for example, page 10 lines 14-15.

New claims 68-73 find support in the specification at, for example, page 3 lines 5-13.

New claims 74-81 find support in the specification and in originally filed claims 13-20.

New claims 85-88 and 94-97 find support at, for example, page 8 lines 20-22 of the specification.

New claims 82, 84 and 89 find support in the specification at, for example, page 13 lines 5-16.

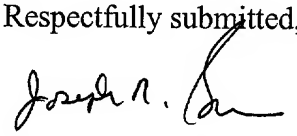
New claims 90-92 find support at, for example, page 13 lines 17-29 of the specification.

New claim 93 finds support in the specification at, for example, page 10 lines 25-33.

CONCLUSION

In view of the foregoing, Applicants respectfully request early action on the merits. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned attorney at (925) 472-5000

Respectfully submitted,



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